Title page

Manuscript title: A mixed methods study of the administration of flucloxacillin oral liquid; identifying strategies to overcome administration issues of medicines with poor palatability

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Abstract:

Background: The palatability of flucloxacillin oral liquid is poor. Parents/carers use strategies to aid administration of poorly palatable medicines.

Aim: To assess views on the palatability of flucloxacillin oral liquid and identify factors associated with successful administration

Methods: A mixed methods study which included a structured review of online forums and a survey of parent/carers of children with Cystic Fibrosis (CF) to obtain parent/carer views on the administration of flucloxacillin oral liquid.

Results: 18 strategies to aid the administration of flucloxacillin suspension to children were identified on 10 different public online forums. 255 responses to the open online survey were received with 47% of respondents reporting that administration of flucloxacilin was more problematic compared to other medicines and 38% reporting the need to improve the palatability. The brand of flucloxacillin oral liquid significantly influenced the degree of difficulty associated with administration to children. A significant relationship was found between the concentration of flucloxacillin and the reported number of doses successfully administered.

The use of food and drink to aid administration was more commonly stated in online forums (44%) compared to the survey data of parents/carers of children with CF (15.9%).

Conclusion: Administration of flucloxacillin oral liquid is perceived as a challenge by parent/carers because of palatability. For chronic use a more concentrated oral liquid and certain brands are likely to improve acceptability.

1. INTRODUCTION

Poor palatability of paediatric medicines has the potential to influence adherence to therapeutic regimens and outcomes (1-3).

Flucloxacillin was the second most commonly prescribed penicillin (following amoxicillin) within the UK in 2012 (4).UK guidelines recommend that babies with cystic fibrosis (CF), should be started on flucloxacillin (125mg twice daily) as antibiotic prophylaxis to prevent airway infection with Staphylococcus aureus (5). The current recommendations suggest this should be until the child is three years of age, although for most UK clinics the antibiotic is continued beyond this age. A trial in healthy child volunteers (conducted in the United States of America) reported that cloxacillin (similar tasting to flucloxacillin) tasted significantly worse than other antibiotics (6). It is widely reported amongst healthcare professionals that flucloxacillin is poorly palatable with recommendations that the child is observed swallowing a dose prior to full prescription (3, 7). Specific issues with flucloxacillin administration to children were identified by healthcare professionals in the UK, with one nurse suggesting giving a sweet (candy) after administration to improve acceptance (8).

The extent to which dosage forms are manipulated to improve taste is unknown. Health professionals previously estimated that 10-30% of people modify their medicines (9). Mixing medicines with food is often undertaken in a paediatric setting to improve palatability, typical foods used within a hospital setting include jam, custard, yogurt, honey, juice and water (10). Data from parents suggest that up to 40% of medicines are mixed with food to improve palatability (11-13). Although mixing medicines into food/drink is common practice by parents and within paediatric wards,(14) there is no evidence base for this manipulation and this is an area where further guidance is required (15). Flucloxacillin stability is pH-dependent, with maximum stability at pH 6.5; and more rapid degradation at lower pH values (16). Therefore the pH of food mixed with flucloxacillin may affect its stability prior to ingestion. Mixing of flucloxacillin with food may impact

on drug stability and absorption, which may reduce efficacy. Sutherland et al (1970) reported a delay in the absorption of flucloxacillin and 50% overall reduction in the concentrations obtained following dosing adults in the fed state compared to the fasting state (17). Bergdahl et al (1986) conducted a study in children that compared the absorption of flucloxacillin in the fed and fasted state, the results did not show significant differences in the overall exposure (of the drug as a result of food in those aged 0.5-4 years however there appeared to be a significant ($p<0.05$) increase in the exposure in those aged 0-1 months in the presence of food, as well as a delay in the Tmax (18). The patient information leaflet for flucloxacillin states that it should be taken half to one hour before food (19-21).

A number of helpful websites have reported strategies to support parent/carers with administration of medicine to children (eg(22-24)). The information is not derived from a clear evidence base and it is difficult to translate this advice to specific populations or medicines (25).

The aim of this study was to assess the extent to which palatability of flucloxacillin oral liquid is a barrier to administration and to compile resources to support parents/carers and improve administration of flucloxacillin oral liquid to children. Administration is linked to acceptability and often easing administration requires improving the acceptability of the medicine to the child. This study links improving acceptability to ease administration throughout.

2. METHODS

2.1. Review of online forums

A systematic search of online forums was conducted using the search terms ‘flucloxacillin’ AND ‘taste’ OR ‘palatability’ OR ‘child’ within a standard google.com search to identify reports of strategies used by parents/carers to aid administration of flucloxacillin to children. Online discussion forum websites were selected based on their popularity and common usage (by looking at the

number of users (where data was available) and the frequency of posts) by the UK population (rather than among specialist interest groups or social media superusers). This type of analysis is classified as passive analysis with low intrusiveness, that is, analysis of information patterns and interactions on discussion groups of which researchers have not been part. Information from these forums was extracted using a template to capture the age of the child; the reason for using flucloxacillin (acute vs chronic use); the reason why flucloxacillin administration was an issue; and the strategy employed by the parent/carer. The acute (treatment for infections) vs chronic (prophylactic treatment) use was assessed by the original post to note the reason for prescribing flucloxacillin; where information was missing this was recorded as not-stated.

2.2. Survey of parents/carers of children with CF

Study design

A bespoke survey was developed based on key questions that were identified by a multidisciplinary team (respiratory consultant; pharmacist; CF patient representative (adult); parent of a child with CF and academic researcher in paediatric medicines); relevant literature and the review of online forums to collect information on strategies that parents currently use or have used previously to aid in the administration of oral liquid flucloxacillin to children with CF.

Participants and Recruitment

For this survey, parent/carers of children with CF were identified as the target population; with inclusion criteria being that the survey participant identifies as caring for a child with CF who has taken oral liquid flucloxacillin (no exclusion criteria). Potential participants were recruited via distribution of the survey uniform resource identifier (URL) via 3-closed CF parent Facebook groups (total of 4840 members) and 2 open CF family Facebook groups (total of 1092 members). It was also shared on Twitter™ by the Cystic Fibrosis Trust (19000 followers) and CF Aware (10000 followers).

Survey Development

The survey was constructed with fixed options as well as free text comments on questions to allow the best quality data to be generated whilst minimising the time burden to participants. Key areas of interest included: strategies used to administer oral liquid flucloxacillin based on the age of the child ranging from a pre-weaned child to an adolescent; the formulation of oral liquid flucloxacillin used (including brand and strength); the extent of the issue of administration of oral liquid flucloxacillin (compared to other medicines); the use of (i) food/drink (ii) devices and (iii) encouragement to aid in the administration of oral liquid flucloxacillin (with a request to include examples). A draft questionnaire was reviewed by the multidisciplinary team to assess ease of completion and ensure that questions were phrased unambiguously. The online survey software, Bristol Online Survey, (www.onlinesurveys.ac.uk) was deemed most appropriate as it is specifically designed for academic research and public sector organisations and is fully compliant with UK data protection laws. A non-probability based convenience sampling method was selected and individuals were left with a choice to "opt in" to the questionnaire following an invitation. A target sample size was not set as this was a consultation and not research therefore statistical powering is not relevant. However, it was felt that at least 200 responses were required to ensure that the results were representative. The survey used in this study was approved by the University of Birmingham Science, Technology, Engineering and Mathematics (STEM) Ethical Review Committee (reference ERN_14-1257). The questionnaire was launched on 3rd February 2015 with an end date of 3rd March 2015.The final survey is included as supplementary file 1.

Data coding and analysis

For closed-ended questions, questionnaire data was translated into numerical code on IBM SPSS statistical software package to allow the results to be analysed in order to assess the significance of patterns and relationships in the data ($p<0.05$ was the cut off for statistical significance). Cross-tabulations and 2x2 tables were used to compare the relationship between questions, with non-parametric chi-square tests being used to analyse the significance of relationships between 2

questions/variables; further, Cramer's V coefficient was calculated to assess the strength of the association between the two variables.

3. RESULTS

3.1. Passive analysis of online forums

Eighteen unique reports on the administration of flucloxacillin oral liquid were identified on 10 different public online forums (Table 1). Details of the online forums included are listed in Box 1. Eight responses recommended mixing flucloxacillin with food/drink. Milk was commonly used for children aged 6-20 months; honey, Nutella®, jam, ice cream and fruit flavoured drinks for those aged 21-36 months. The use of an oral syringe to direct the medicine slowly into the back/side of the mouth was also reported as a method to ease administration compared to the medicine spoon supplied with the product. The use of rewards following administration of flucloxacillin was reported, with most being food-based.

Table 1. Reports identified on public online forums to aid the administration of flucloxacillin to children

The unpleasant taste of flucloxacillin was described in several forums, examples of such statements include:

"It's absolutely rancid and I don't know why they offer it to young children" (Netmums contributor)

"Floxapen brand of flucloxacillin actually tastes quite nice, it's the other unbranded stuff that's vile for some reason" (Damsels: the women's network contributor)

3.2. Survey responses from parents/carers of children with CF

255 responses to the questionnaire were received, 8 responses (3%) were received from outside of the UK. Only 2 respondents reported that their child had never previously taken and was not currently taking flucloxacillin oral liquid; their answers were removed from the analysis.

47% of parents/carers reported the administration of flucloxacillin was more problematic than other medicines. Of those who answered 'more' (n=119), the majority (73.1%) of parents/carers reported that it was the taste of flucloxacillin which made it more difficult to administer. In addition, 30.2% of parents/carers answering 'more' stated that their child would spit out the medicine, retch or vomit. Administration was the greatest issue in pre-weaned children as shown in Table 2.

Table 2. Impact of child's age on the parents/carers response to 'Compared to other medicines you have had to administer to your child, do you/did you find the administration of flucloxacillin more or less problematic?'

llustrative quotes from parents regarding the impact of age on administration of flucloxacillin liquid are provided below, these quotes suggest that as the child gets older administration becomes less of an issue for children with CF.

"Initially it was very, very difficult, however, my daughter eventually got used to it" (Participant 91)

"Initially when our daughter was a tiny baby, it was by far the most difficult to give. She is now 3 and actually likes it though!" (Participant 12)

"The taste was unbearable. I think he managed the sugar-free version in the end and I suppose after a year of administration he got used to the taste" (Participant 196)

Chi-square analysis revealed a strong relationship between the responses to the question 'To what extent do you agree with the statement 'I find/found the administration of flucloxacillin

problematic?' and 'How many of the recommended doses of flucloxacillin do you/did you manage to successfully administer?' ($\chi 2 = 78.5$; $p<0.001$; Cramer's V=0.40). The majority (89.3%) of parent/carers reported that they administer/administered 'most doses' or 'all doses' of flucloxacillin. There were 36 reports that a child spat out the medicine, retched or vomited which suggest over reporting of achieving most or all doses. The questionnaire did not define administration as swallowing the complete dose, therefore some parents may interpret administering all doses as providing them to the child yet not ensuring that the child swallowed the medicine.

49% of respondents were unaware of the flucloxacillin brand that they administered to their child. A significant relationship was found between the brand of flucloxacillin administered and whether parents/carers agreed or disagreed with the statement 'I find/found the administration of flucloxacillin problematic' ($\chi 2 = 11.2$; $p=0.047$). Cramer's V analysis implied a moderate association (V= 0.21) where parents/carers administering Crescent Pharma and Medreich brands were least likely to agree that flucloxacillin administration is problematic (data shown in figure 1). Some parents referred to Floxapen brand of flucloxacillin which was withdrawn in 2009 (29). A full list of brands available together with the flavouring agents used in each product is included in as supplementary material 2.

Figure 1. The percentage of parents/carers for each brand of flucloxacillin administered reporting 'agree' or 'strongly agree' in answer to the question, 'To what extent do you agree with the statement 'I find/found the administration of flucloxacillin problematic'?

A significant relationship was found between the concentration of oral liquid and the number of doses successfully administered ($\chi 2 = 10.3$; $p=0.035$). Only 6% of parents administering the stronger strength product (250mg/5mL) reported administering 'no' or 'some doses' in comparison with 12% of parent/carers administering 125mg/5mL. The increase in acceptability of the more concentrated

flucloxacillin product may be correlated with the increased age of the child as older children are more likely to be prescribed the stronger product, however, our data did not allow this analysis due to the sample size.

Example quotes from parents are included to highlight these findings related to specific products.

"Had the same brand for a while..child took it no bother..now it's this new one he's not too keen!!" (Participant 144)

"It was the most problematic when she was on the lower strength, so therefore more {volume} and sugar-free. She now takes the 250mg/5ml normal (not sugar free) fine" (Participant 182)

"Giving less with stronger strength and sticking with the sugar variety helped" (Participant 201)

"My daughter is now on capsules she is 6 but taken capsules since aged 3" (Participant 34)

"Our hospital started my son on capsules before the age of 4 which has made things much easier" (Participant 77)

16% of parent/carers reported that mixing with food/drink eased the administration of flucloxacillin. However a further 13% reported that mixing with food or drink did not help with administration. Furthermore, it was reported by 4% of parents/carers who had mixed with food/drink that the child would actually refuse to then consume the food or drink in the future. Chi-square analysis found a significant relationship between mixing with food/drink and whether the parents/carer found flucloxacillin administration problematic ($\chi 2=22.7$; $p<0.001$), with a strong relationship between the two (Cramer's V=0.30). Based on the odds ratio, those who mixed with food/drink were 3.1 times more likely to describe administration as problematic. The different foods/drinks that were recommended changed with age where milk was used in pre-weaned babies and also being recommended for children up to 5 years old. In children aged 3-11, mixing with juice was popular, with hot chocolate also being described. Yoghurt was mentioned for all age groups that were weaned. Illustrative quotes from parents/carers regarding the co-administration of flucloxacillin liquid with food or drink highlight common issues identified.

"I tried to give with food, and even mix into drink, but it didn't help" (Participant 43)

“I give it while she's drinking her bottle as she sucks and takes it without realising but she's getting better at taking it straight from a syringe if in a good mood” (Participant 101)

“We tried to mix with yoghurt. He now won't eat yoghurt because he thinks it tastes like that.” (Participant 121)

“We were told by our nurse that it should not be added to milk or given with milk as that affected its potency. So we didn't do it.” (Participant 136)

51% of parent/carers provided current/former strategies used to aid the administration of flucloxacillin oral liquid in pre-weaned babies. The most common strategy for pre-weaned babies was to use an oral syringe (and not the medicine spoon supplied); where flucloxacillin is administered slowly into the side or corner of the mouth. The use of a medicine dummy (soother medicine dispenser) and bottle teat were also described as strategies for the younger age groups. 15.8% of parents/carers found that encouragement was helpful in the administration of flucloxacillin as children were older. The most commonly reported ways to encourage children to take flucloxacillin were praise (16.3% of parents/carers), sweets (16.3% of parents/carers) and stickers (12.7% of parents/carers).

All survey participants were invited to provide any comments on how the administration of flucloxacillin could be improved and 162 of the 254 (64%) participants chose to respond. Table 3 shows common themes.

There were many negative comments made within this section, illustrated by,

“..it’s very traumatic for a parent with a newly diagnosed (CF) child to have to deal with trying to force this (flucloxacillin) down their throat” (Participant 15)

Table 3. Themed strategies reported to improve administration of flucloxacillin oral liquid (n=162 in total; n>5 was required for a topic to be considered a theme).

Over a third (38.3%) of parents/carers in this study reported that they thought administration of flucloxacillin could be eased by a more pleasant taste or flavour. 11.1% parents/carers of children with CF recommended moving from the flucloxacillin oral liquid to capsules to avoid the issue with taste and 7 parents/carers reported children starting taking flucloxacillin capsules between 18 months and 4 years of age.

4. DISCUSSION

Main Findings

This study supports previous reports of the poor palatability of flucloxacillin oral liquid with several unprompted internet based reports of difficulties in administration to children and 34% of parent/carers of children with CF reporting that taste makes administration of flucloxacillin more problematic than other medicines. Online forum data revealed that administration issues were most common in children 3 years or younger; this was supported by findings from the survey of parents/carers of children with CF who identified that the issues around administration are greatest in the youngest children. The most problematic age group for the administration of flucloxacillin oral liquid was reported to be pre-weaned babies; therefore strategies to aid administration in this age group are likely to be particularly beneficial.

Strengths and limitations

This is the first study to collect data on parent/carer strategies on the delivery of flucloxacillin oral liquid to children. Online forums are useful sources of information regarding medicines administration although the authors recognise that only serious issues are likely to be raised and this may introduce some bias into the results. However, in identification of parent strategies in administration of flucloxacillin it is the responses to the originator post that are of most interest. The use of a survey to parents/carers of children with CF provided a means to gather data from a

population known to be experienced in the administration of flucloxacillin oral liquid to children; however, it is acknowledged that the survey used free text responses to explore the reasons why administration was problematic rather than quantifying all possible reasons. This approach was selected to minimise bias and allow parents/carers to provide information on all aspects of administration rather than being prompted by the use of potentially leading questions.

It is acknowledged that parents/carers experiencing an issue with the administration of flucloxacillin are more likely to respond to a survey, however, as the results will be used to develop a support package for parents/carers that do experience an administration issue this population selection is appropriate.

The use of an online survey provides wide reach into the CF population as it can be distributed easily and parents/carers have the option to opt in without pressure, however, it will only reach those parents/carers who are active in a CF social media network which was a recognised limitation of the study. This approach to distribution of the survey was selected as a link or message from an existing contact is typically less likely to be deleted or ignored. The distribution was centered around the UK CF population although the facebook groups and twitter accounts are open to other parents/carers/patients with CF globally, however, they are likely only to be accessed in English speaking countries. Although this was a qualitative study with nonprobability sampling techniques where the sample size is not critical, an estimate of the number of children with CF in the UK is 4500 (Clinical guidelines: care of children with cystic fibrosis 2014); therefore the participants represent ~5% of the total population within the UK.

What is already known on this topic

Previous reports of adherence to oral antibiotics are approximately 50% for four times daily dosing (as with flucloxacillin prescribed for acute infections) and ~70% for twice daily administration as in CF patients (26). However, there is evidence that parents over report compliance to medication (eg

(27, 28)). This study found that almost 90% of parents/carers reported administering all or most of the doses of oral liquid flucloxacillin to their child which is higher than previous reports.

It is already known that nurses to use food/drink to mix with medicines within a ward setting (14) and there are previous reports of parents mixing medicines with food and drink with values of up to 40% of medicines being mixed with food/drink (12, 13). The online forums primarily reported strategies used to aid administration of flucloxacillin oral liquid to children with an acute illness and the use of food as a co-administration aid to improve palatability was more common that reports from parents/carers of children with CF (a chronic illness). However, although mixing medicines into food/drink is common practice there is no evidence base for this manipulation and that this is an area where further guidance would be beneficial as messages to parents/carers are often confusing and there is no evidence base to support co-administration of flucloxacillin with food (15). The lower incidence of using food as a co-administration aid in children with CF may be attributed to the comparative medicines related knowledge base of parents with a chronically ill child compared to those with a child with an acute illness. Further research is needed to evaluate the consequences of co-administration of flucloxacillin with food (15).

Taste is one of the most common barriers to administration of medicines to children (3), this may be why the administration of flucloxacillin becomes easier with age, as the child can swallow a capsule which removes the issue of taste. The age at which children convert to capsules was not recorded in this study. The Summary of Product characteristics for flucloxacillin capsules does not have an age where these are considered appropriate, however, the minimum dose of 250mg suggests that this would only be appropriate for the treatment of certain children as, for example, the dose banding does not permit treatment for primary prevention of *Staphylococcus aureus* lung infection in cystic fibrosis (125mg twice daily).

Implications for practice and recommendations

Information gathered from parents and carers on strategies to aid administration of oral liquid flucloxacillin to children can be used to advise other parents/carers on the administration of flucloxacillin and other poorly palatable medicines to children.

The parent/carer recommendations within this study include:

- The use of an oral syringe was commonly reported to improve issues around administration within the online forums; this is a standard medical device and is commonly used in the administration of liquid medicines to children; however, the ability to direct the medicine more accurately than using a spoon seems to be of benefit to children. Typically flucloxacillin is supplied with a spoon and not an oral syringe.
- Using a higher strength product reduces the volume to be administered and this appears to have a beneficial impact on administration.
- Certain brands were also highlighted as having fewer issues (Medreich and Crescent); however it is not clear why these brands are preferred. The flavours used in the more popular brands are pineapple and menthol in Medreich and cherry in Crescent; Actavis brand which was the least popular uses menthol, lemon and strawberry as flavouring agents and Milpharm another less popular brand uses pineapple and menthol (as Medreich) (full details of all formulations are included in supplementary file 2).
- Parents faced with long-term administration should seek advice from their pharmacy with respect to identifying a preferred flucloxacillin brand and maintaining that supply.
- Co-administration with food was reported to improve administration when flucloxacillin was indicated for the treatment of acute illnesses. However, it is not possible to provide any advice on foods that were more or less successful as the survey was not designed to answer this question.

5. CONCLUSION

Administration of flucloxacillin oral liquid to children can be a challenge and parent/carers should be supported with this task. Previous knowledge of the impact of food on the bioavailability of flucloxacillin in children is not conclusive (18). Regular reports of mixing flucloxacillin with food highlights the need for additional research to understand the impact on pharmacokinetics of co-administration with food to improve palatability rather than dosing with a full meal. These data demonstrate the need for production of more palatable paediatric formulations of flucloxacillin. It is important that manufacturers and regulators aid the development of more palatable medicines for children where possible.

These data will facilitate the production of resources to support parents/carers in the administration of flucloxacillin (and other unpalatable medicines) highlighting the importance of a positive attitude; persistence; and specific strategies relating to the product brand and concentration. These resources may have important implications for the delivery of future clinical trials and to improve adherence to poorly palatable medicines used in paediatric practice.

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Table 1. Reports identified on public online forums to aid the administration of flucloxacillin to children

Patient Characteristics		Strategy Reported			
Age of child (months)	Treatment duration	Mixed with food/drink	Device used	Reward	Other methods
6	Chronic	Milk			
6	Not stated		Syringe		Sing songs
8	Acute				Dip syringe in Calpol®
15	Not stated		Syringe		Pretend to give to pet
15	Acute		Syringe	Fruit pastille	
20	Acute	Formula milk			
20	Acute		Syringe		
21	Acute	Honey			
22	Acute		Syringe		
24	Acute			Magic stars	
24	Acute	Yoghurt, Nutella	Syringe		
24	Acute			Yoghurt	
36	Acute	Jam, yoghurt, honey, fruit flavoured drink, Vimto	Syringe		
36	Acute	Calpol®, milk, sugar			
36	Acute	Ice cream	Syringe		
36	Acute	Fruit flavoured drink		Chocolate fudge	
84	Acute				Drink of water after
120	Acute			Sweets/fizzy drink	

Table 2. Impact of child's age on the parents/carers response to 'Compared to other medicines you have had to administer to your child, do you/did you find the administration of flucloxacillin more or less problematic?'

		How problematic compared to other drugs (% of parents/ carers)		
	n	More	Less	No different
Pre weaning	21	90.4	4.8	4.8
Post weaning - 2 years	80	42.4	11.3	46.3
3-5 years	68	50.0	13.2	36.8
6-11 years	61	36.1	4.9	59.0
12-17 years	23	43.5	17.4	39.1

Table 3. Themed strategies reported to improve administration of flucloxacillin oral liquid (n=162 in total; n>5 was required for a topic to be considered a theme).

Strategy	Frequency
Improve the taste/flavour of the product	62
A positive parent/carer attitude	18
Identify a favourite brand	13
Use a sugar-containing brand	9
Move onto the capsule product as soon as the child is able to swallow this product	18

Figure 1. The percentage of parents/carers for each brand of flucloxacillin administered reporting 'agree' or 'strongly agree' in answer to the question, 'To what extent do you agree with the statement 'I find/found the administration of flucloxacillin problematic'?

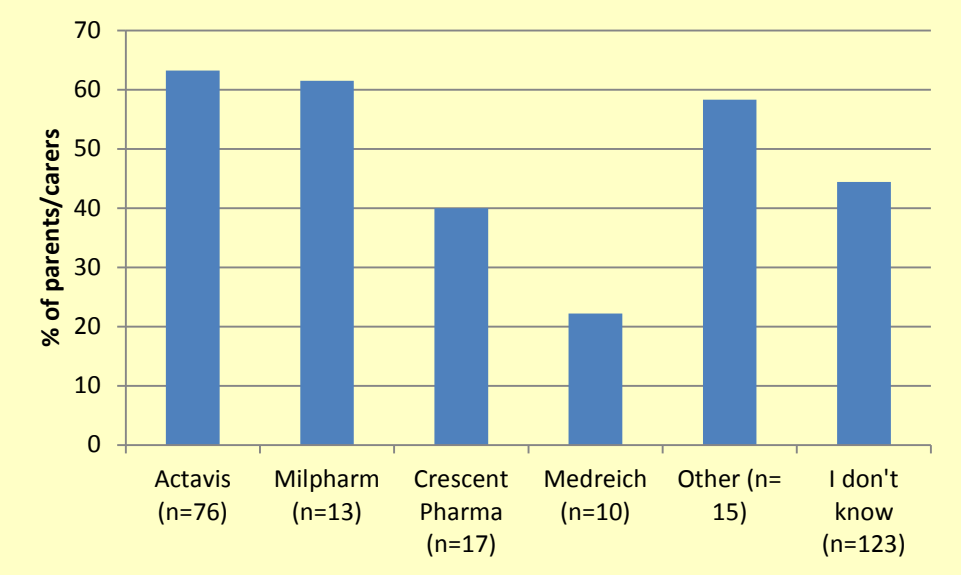

Figure 2. Illustrative transcripts from parent/carers of children with CF on the use of food/drink to aid administration of flucloxacillin oral liquid.

"I tried to give with food, and even mix into drink, but it didn't help"

"I give it while she's drinking her bottle as she sucks and takes it without realising but she's getting better at taking it straight from a syringe if in a good mood"

"We tried to mix with yoghurt. He now won't eat yoghurt because he thinks it tastes like that."

"We were told by our nurse that it should not be added to milk or given with milk as that affected its potency. So we didn't do it."

Figure 3. Illustrative transcripts from parents/carers of children with CF on the impact of age on administration of flucloxacillin oral liquid

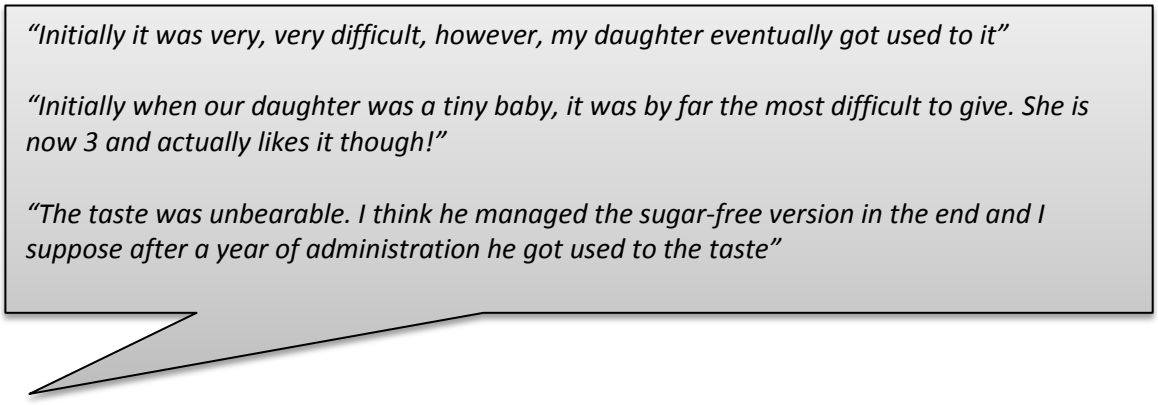

Figure 4. Illustrative transcripts from parent/carers of children with CF on the impact of flucloxacillin oral liquid product on administration

"Had the same brand for a while..child took it no bother..now it's this new one he's not too keen!!"

"It was the most problematic when she was on the lower strength, so therefore more {volume} and sugar-free. She now takes the 250mg/5ml normal (not sugar free) fine"

"Giving less with stronger strength and sticking with the sugar variety helped"

"My daughter is now on capsules she is 6 but taken capsules since aged 3"

"Our hospital started my son on capsules before the age of 4 which has made things much easier"

Box 1. Online forums included

- Mumsnet (www.mumsnet.com)
- Netdoctor (www.netdoctor.co.uk)
- Netmums (www.netmums.com)
- Bub Hub (www.bubhub.com)
- Cystic Fibrosis Trust Forum (http://forum.cysticfibrosis.org.uk/)
- Treasures (www.treasures.co.nz)
- HealthUnlocked (www.healthunlocked.com)
- BabyCentre (www.babycentre.co.uk)
- Yahoo Answers (https://uk.answers.yahoo.com/)
- Damsels: the women's network (www.damsels.org)
- Frightful Bish (https://frightfulbish.wordpress.com/)

Supplementary file 1. Final survey distributed to parents/carers of children with CF.

Question	**Answer options**
Please confirm whether you care/cared for a child with cystic fibrosis aged 17 or younger.	Yes/No
Please confirm whether your child has previously taken/is currently taking liquid oral flucloxacillin?	Yes/No
Please select the age of your child.	Pre weaning Post weaning- 2 years 3-5 years 6-11 years 12-17 years
Please identify the brand of flucloxacillin administered (the brand and/or concentration of the flucloxacillin will usually be printed on the box or the bottle).	Actavis Aurobindo Milpharm I don't know Other (please state)
Please identify the strength of flucloxacillin administered	125mg/5mL 250mg/5mL I don't know
Were you asked whether you would prefer one brand/concentration of flucloxacillin rather than another? If 'yes', please write whether you did or did not request a particular brand or concentration and give the reason(s) why. *(Optional)*	Yes/No *Free text*

Compared to other medicines you have had to administer to your child, do you/did you find the administration of flucloxacillin more or less problematic? If you answered 'more', please briefly explain why in the box below	More Less No different *Free text*
To what extent do you agree with the statement 'I find/found the administration of flucloxacillin problematic'?	Strongly disagree Disagree Agree Strongly agree
How many of the recommended doses of flucloxacillin do you/did you manage to successfully administer?	No doses Some doses Most doses All doses
To what extent do you agree with the statement 'mixing flucloxacillin with food and/or drink eases/eased its administration'?	Strongly disagree Disagree Agree Strongly agree
Do you/did you ever use food or drink to aid in the administration of flucloxacillin? If you answered 'yes', please list any food and/or drink you have used in the box below with any additional comments or preferences.	Yes/No *Free text*
If your child is currently breast/bottle fed, what strategies do you use to aid the administration of flucloxacillin?	*Free text*

If your child is weaned, please give details in the box below of strategies you remember using to aid the administration of flucloxacillin when your child was still being breast/bottle fed (e.g. mixing with anything, what device worked best). (Optional)	
What delivery device do you/did you find most successful for the administration of flucloxacillin?	Spoon Oral syringe into the side of mouth (cheek) Oral syringe into the back of the mouth Oral syringe onto the tongue Other (please specify)
Do you/did you find encouragement (e.g. the use of sticker charts or treats) useful in the administration of flucloxacillin? If you answered 'yes', please give details in the box below	Yes/No *Free text*
Please give any other comments or ideas about how the administration of flucloxacillin could be improved/eased.	*Free text*

Supplementary file 2.

Oral liquid flucloxacillin products currently available in the UK. Presented information is from the Summary of Product Characteristics for each product.

Medicine name	Active Ingredient	Flavouring	Sweetening agent	Company name
Flucloxacillin 125mg/5ml and 250mg/5ml Sugar-Free Powder for Oral Solution	Flucloxacillin sodium	Menthol, lemon, strawberry	Sorbitol	Actavis UK Ltd
Flucloxacillin 125mg/5ml Oral solution	Flucloxacillin sodium	Pineapple, menthol	Sucrose	Milpharm Ltd
Flucloxacillin 125mg/5ml Sugar-Free Powder for Oral Solution	Flucloxacillin sodium	Menthol, lemon, strawberry	Sorbitol	Actavis UK Ltd
Flucloxacillin 250/5ml Sugar Free Oral Solution	Flucloxacillin sodium	Menthol, lemon, strawberry	Sorbitol	Actavis UK Ltd
Flucloxacillin 125mg/5mL Powder for Oral Solution	Flucloxacillin sodium	Pineapple, Menthol	Sucrose	Medreich PLC
Flucloxacillin 125 mg/5ml Granules for Oral Solution	Flucloxacillin sodium	Cherry	Sucrose	Crescent Pharma Ltd
Flucloxacillin 250 mg/5ml Granules for Oral Solution	Flucloxacillin sodium	Cherry	Sucrose	Crescent Pharma Ltd

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Flucloxacillin 125mg/5ml Sugar-Free Powder for Oral Solution	Flucloxacillin sodium	Menthol, lemon, strawberry	Sorbitol	Actavis UK Ltd
Flucloxacillin 250/5ml Sugar Free Oral Solution	Flucloxacillin sodium	Menthol, lemon, strawberry	Sorbitol	Actavis UK Ltd
Flucloxacillin 125mg/5mL Powder for Oral Solution	Flucloxacillin sodium	Pineapple, Menthol	Sucrose	Medreich PLC
Flucloxacillin 125 mg/5ml Granules for Oral Solution	Flucloxacillin sodium	Cherry	Sucrose	Crescent Pharma Ltd
Flucloxacillin 250 mg/5ml Granules for Oral Solution	Flucloxacillin sodium	Cherry	Sucrose	Crescent Pharma Ltd